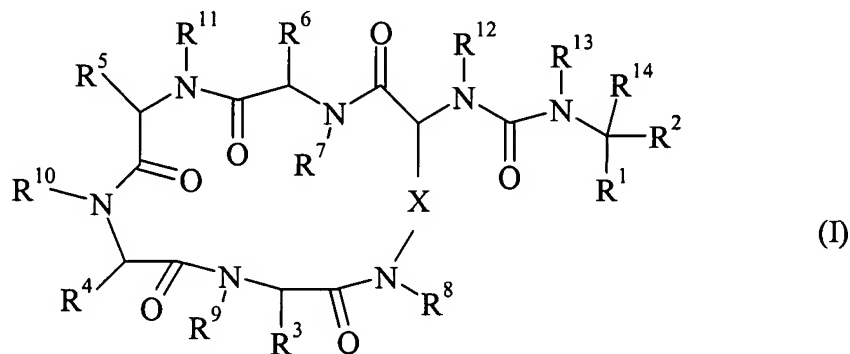


**IN THE CLAIMS:**

Claim 1 (**currently amended**): A method for the treatment or prophylaxis of a disease or medical condition wherein inhibition of carboxypepsidase U is beneficial, said method comprising administering to a warm-blooded animal in need thereof an effective amount~~The use~~ of a compound of formula (I):



wherein:

X is (CH<sub>2</sub>)<sub>m</sub>Y(CH<sub>2</sub>)<sub>n</sub>;

m and n are, independently, 1, 2, 3, 4, 5 or 6; provided that m + n is not more than 6;

Y is a bond, O, S(O)<sub>p</sub>, or S-S;

R<sup>1</sup> is CO<sub>2</sub>R<sup>15</sup> or a carboxylic acid isostere such as S(O)<sub>2</sub>OH, S(O)<sub>2</sub>NHR<sup>15</sup>, PO(OR<sup>15</sup>)OH, PO(OR<sup>15</sup>)NH<sub>2</sub>, B(OR<sup>15</sup>)<sub>2</sub>, PO(R<sup>15</sup>)OH, PO(R<sup>15</sup>)NH<sub>2</sub> or tetrazole;

R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are, independently, hydrogen, C<sub>1-6</sub> alkyl (optionally substituted by halogen, hydroxy, cyano, SH, S(O)<sub>3</sub>H, S(O)<sub>q</sub>(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-4</sub> alkyl), CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, COOH, CONH<sub>2</sub>, CONH(C<sub>1-6</sub> alkyl), NH<sub>2</sub>, CNH(NH<sub>2</sub>), or NHCNH(NH<sub>2</sub>)), C<sub>3-6</sub> cycloalkyl(C<sub>1-4</sub>)alkyl (wherein the cycloalkyl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)), heterocyclyl(C<sub>1-4</sub>)alkyl (wherein the heterocyclyl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)), phenyl(C<sub>1-4</sub>)alkyl (wherein the phenyl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)) or heteroaryl(C<sub>1-4</sub>)alkyl (wherein the heteroaryl ring is

optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>));

p and q are, independently, 0, 1 or 2;

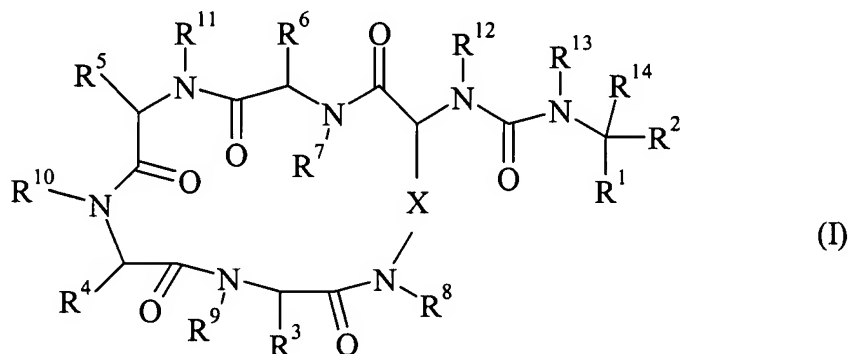
R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are, independently, H or C<sub>1-4</sub> alkyl;

R<sup>14</sup> is H or C<sub>1-4</sub> alkyl; and,

R<sup>15</sup> is H or C<sub>1-4</sub> alkyl;

or a pharmaceutically acceptable salt thereof, or solvate thereof, or a solvate of such a salt; in a method of manufacturing a medicament for the treatment or prophylaxis of a condition wherein inhibition of carboxypeptidase U is beneficial.

Claim 2 (currently amended): A compound of formula (I):



wherein:

X is (CH<sub>2</sub>)<sub>4</sub>;

R<sup>1</sup> is CO<sub>2</sub>R<sup>15</sup>;

R<sup>2</sup> is C<sub>1-6</sub> alkyl, benzyl, straight-chain C<sub>1-6</sub> alkyl substituted at its terminus by NH<sub>2</sub>,

CNH(NH<sub>2</sub>)<sub>1-6</sub> or NHCNH(NH<sub>2</sub>) or (6-aminopyridin-3-yl)methyl; C<sub>3-6</sub> cycloalkyl substituted by NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); heterocyclyl containing at least one nitrogen atom; non-nitrogen containing heterocyclyl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); heteroaryl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); phenyl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); heteroaryl(C<sub>1-4</sub>)alkyl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); phenyl(C<sub>1-4</sub>)alkyl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); or C<sub>3-6</sub> cycloalkyl(C<sub>1-4</sub>)alkyl substituted with NH<sub>2</sub>,

CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); all of the above rings being optionally further substituted by one or more of: halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy or OCF<sub>3</sub>; one of R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is independently, hydrogen, heteroaryl(C<sub>1-4</sub>)alkyl (wherein the heteroaryl ring is optionally substituted by one or more of halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)); and the others are, independently, hydrogen, C<sub>1-6</sub> alkyl (optionally substituted by halogen, hydroxy, cyano, SH, S(O)<sub>3</sub>H, S(O)<sub>q</sub>(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-4</sub> alkyl), CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, COOH, CONH<sub>2</sub>, CONH(C<sub>1-6</sub> alkyl), NH<sub>2</sub>, CNH(NH<sub>2</sub>), or NHCNH(NH<sub>2</sub>)), C<sub>3-6</sub> cycloalkyl(C<sub>1-4</sub>)alkyl (wherein the cycloalkyl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)), heterocyclyl(C<sub>1-4</sub>)alkyl (wherein the heterocyclyl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)), phenyl(C<sub>1-4</sub>)alkyl (wherein the phenyl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)) or heteroaryl(C<sub>1-4</sub>)alkyl (wherein the heteroaryl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)); p and q are, independently, 0, 1 or 2; R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are, independently, H or C<sub>1-4</sub> alkyl; R<sup>14</sup> is H or C<sub>1-4</sub> alkyl; and, R<sup>15</sup> is H or C<sub>1-4</sub> alkyl;

or a pharmaceutically acceptable salt thereof or solvate thereof, ~~or a solvate of such a salt.~~

Claim 3 (**currently amended**): ~~A~~ The compound of formula (I) ~~or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt.~~ as claimed in claim 2 wherein:

X is (CH<sub>2</sub>)<sub>4</sub>;

R<sup>1</sup> is CO<sub>2</sub>R<sup>15</sup>;

R<sup>2</sup> is straight-chain C<sub>1-6</sub> alkyl substituted at its terminus by NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); C<sub>3-6</sub> cycloalkyl substituted by NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); heterocyclyl containing at least one nitrogen atom; non-nitrogen containing heterocyclyl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); heteroaryl substituted with NH<sub>2</sub>,

CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); phenyl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); heteroaryl(C<sub>1-4</sub>)alkyl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); phenyl(C<sub>1-4</sub>)alkyl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); or C<sub>3-6</sub> cycloalkyl(C<sub>1-4</sub>)alkyl substituted with NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>); all of the above rings being optionally further substituted by one or more of: halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy or OCF<sub>3</sub>;

one of R<sup>3</sup>, R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> is independently, hydrogen, heteroaryl(C<sub>1-4</sub>)alkyl (wherein the heteroaryl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)); and the others are, independently, hydrogen, C<sub>1-6</sub> alkyl (optionally substituted by halogen, hydroxy, cyano, SH, S(O)<sub>3</sub>H, S(O)<sub>q</sub>(C<sub>1-6</sub> alkyl), OC(O)(C<sub>1-4</sub> alkyl), CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, COOH, CONH<sub>2</sub>, CONH(C<sub>1-6</sub> alkyl), NH<sub>2</sub>, CNH(NH<sub>2</sub>), or NHCNH(NH<sub>2</sub>)), C<sub>3-6</sub> cycloalkyl(C<sub>1-4</sub>)alkyl (wherein the cycloalkyl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)), heterocyclyl(C<sub>1-4</sub>)alkyl (wherein the heterocyclyl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)), phenyl(C<sub>1-4</sub>)alkyl (wherein the phenyl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>)) or heteroaryl(C<sub>1-4</sub>)alkyl (wherein the heteroaryl ring is optionally substituted by halogen, hydroxy, cyano, C<sub>1-4</sub> alkyl, CF<sub>3</sub>, C<sub>1-4</sub> alkoxy, OCF<sub>3</sub>, NH<sub>2</sub>, CNH(NH<sub>2</sub>) or NHCNH(NH<sub>2</sub>));

p and q are, independently, 0, 1 or 2;

R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are, independently, H or C<sub>1-4</sub> alkyl;

R<sup>14</sup> is H or C<sub>1-4</sub> alkyl; and,

R<sup>15</sup> is H or C<sub>1-4</sub> alkyl;

or a pharmaceutically acceptable salt thereof or solvate thereof, or a solvate of such a salt.

Claim 4 (currently amended): A ~~The~~ compound of formula (I) ~~or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt~~ as claimed in claim 2 ~~or 3~~ wherein:

R<sup>1</sup> is CO<sub>2</sub>R<sup>15</sup>;

$R^2$  is straight-chain  $C_{1-6}$  alkyl substituted at its terminus by  $NH_2$ ,  $CNH(NH_2)$  or  $NHCNH(NH_2)$ ;  $C_4$  alkyl (such as  $CH(CH_3)CH_2CH_3$  or  $CH_2CH(CH_3)_2$ ); or (aminopyridinyl)methyl (for example (6-aminopyridin-3-yl)methyl); one of  $R^3$  and  $R^4$  is (indol-3-yl) $CH_2$  optionally substituted by halo or hydroxy; and the other is benzyl (optionally substituted by halo or hydroxy) or  $C_4$  alkyl (such as  $CH(CH_3)CH_2CH_3$  or  $CH_2CH(CH_3)_2$ ); or  $R^3$  and  $R^4$  are both methyl;  $R^5$  and  $R^6$  are, independently,  $C_{1-6}$  alkyl (for example  $CH_3$ ,  $CH(CH_3)_2$ ,  $CH(CH_3)CH_2CH_3$  or  $CH_2CH(CH_3)_2$ );  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{11}$ ,  $R^{12}$ ,  $R^{13}$  and  $R^{14}$  are H;  $R^{10}$  is  $C_{1-4}$  alkyl; and,  $R^{15}$  is H or  $C_{1-4}$  alkyl;

or a pharmaceutically acceptable salt thereof.

Claim 5 (**currently amended**): The method of claim 1 ~~A compound as claimed in any one of claims 2 to 4~~ wherein X is  $(CH_2)_4$ .

Claim 6 (**currently amended**): The method of claim 1 ~~A compound as claimed in any one of claims 2 to 5~~ wherein  $R^1$  is  $CO_2R^{15}$  in which  $R^{15}$  is H or  $C_{1-4}$  alkyl.

Claim 7 (**currently amended**): A ~~The compound as claimed in claim 2~~ ~~any one of claims 2 to 6~~ wherein  $R^2$  is straight-chain  $C_{1-6}$  alkyl substituted at its terminus by  $NH_2$ ,  $CNH(NH_2)$  or  $NHCNH(NH_2)$ ;  $C_4$  alkyl (such as  $CH(CH_3)CH_2CH_3$  or  $CH_2CH(CH_3)_2$ ); or (aminopyridinyl)methyl.

Claim 8 (**currently amended**): A ~~The compound as claimed in claim 2~~ ~~any one of claims 2 to 4~~ wherein  $R^2$  is  $C_{1-6}$  alkyl ( $CH(CH_3)CH_2CH_3$  or  $CH_2CH(CH_3)_2$ ), benzyl, or straight-chain  $C_{1-6}$  alkyl substituted at its terminus by  $NH_2$ ,  $CNH(NH_2)$ ,  $NHCNH(NH_2)$  or (6-aminopyridin-3-yl)methyl.

Claim 9 (**currently amended**): A ~~The~~ compound as claimed in claim 2 ~~any one of claims 2 to 8~~ wherein  $R^2$  is straight-chain  $C_{1-6}$  alkyl substituted at its terminus by  $NH_2$ ,  $CNH(NH_2)$ ,  $NHCNH(NH_2)$  or (6-aminopyridin-3-yl)methyl.

Claim 10 (**currently amended**): A ~~The~~ compound as claimed in claim 2 ~~any one of claims 2 to 10~~ wherein  $R^3$  is  $CH_2indolyl_1$ -(wherein the indolyl is optionally substituted by one or more of: halogen or hydroxy,  $C_{1-4}$  alkyl or benzyl (optionally substituted by halogen or hydroxy)).

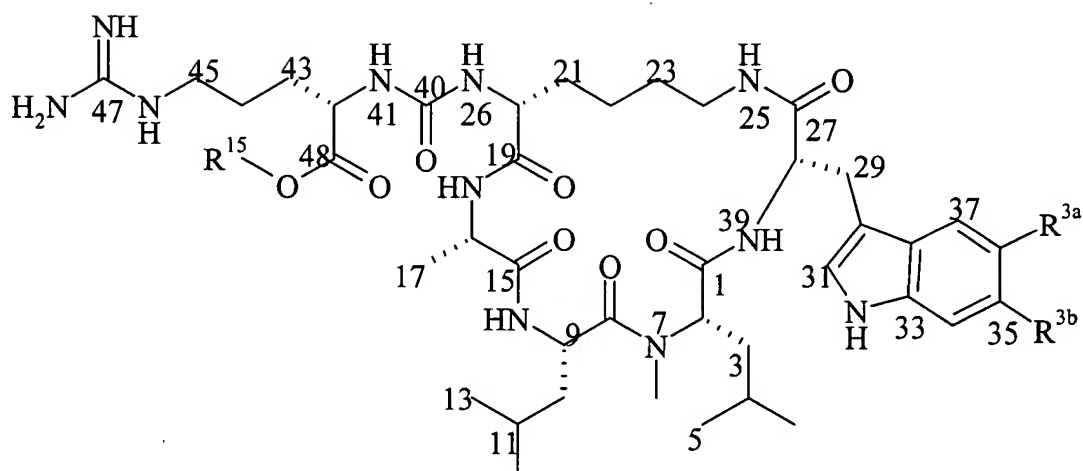
Claim 11 (**currently amended**): A ~~The~~ compound as claimed in claim 2 ~~any one of claims 2 to 10~~ wherein  $R^4$  is  $CH_2indolyl_1$ -(wherein the indolyl is optionally substituted by one or more of: halogen or hydroxy,  $C_{1-6}$  alkyl ( $CH(CH_3)CH_2CH_3$  or  $CH_2CH(CH_3)_2$ ) or benzyl (optionally substituted by halogen or hydroxy)).

Claim 12 (**currently amended**): A ~~The~~ compound as claimed in claim 2 ~~any one of claims 2 to 11~~ wherein  $R^5$  and  $R^6$  are, independently,  $C_{1-6}$  alkyl (~~such as methyl, iso-propyl,  $CH(CH_3)CH_2CH_3$  or  $CH_2CH(CH_3)_2$~~ ).

Claim 13 (**currently amended**): A ~~The~~ compound as claimed in claim 2 ~~any one of claims 2 to 12~~ wherein  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{11}$ ,  $R^{12}$ ,  $R^{13}$  and  $R^{14}$  are all H.

Claim 14 (**currently amended**): A ~~The~~ compound as claimed in claim 2 ~~any one of claims 2 to 4~~ wherein  $R^{10}$  is  $C_{1-4}$  alkyl.

Claim 15 (**currently amended**): A ~~The~~ compound as claimed in claim 2 which is a compound of the following formula



in which

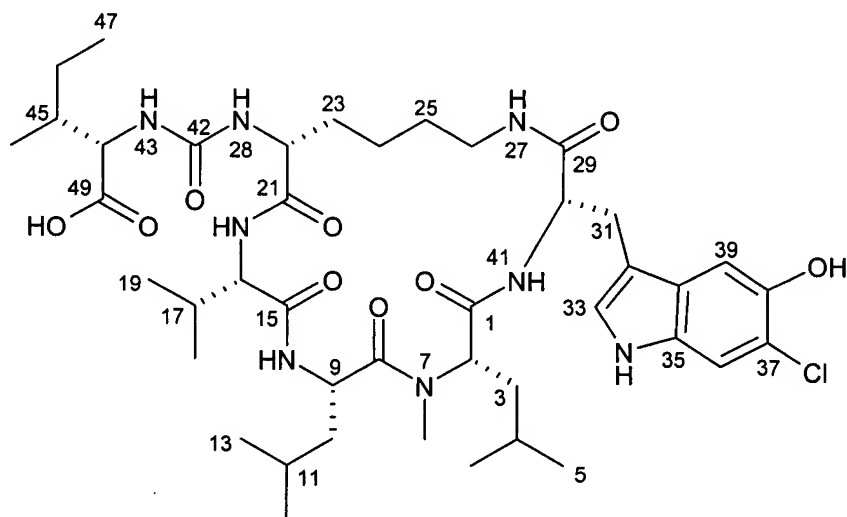
$R^{3a}$  is H,  $R^{3b}$  is H and  $R^{15}$  is H;

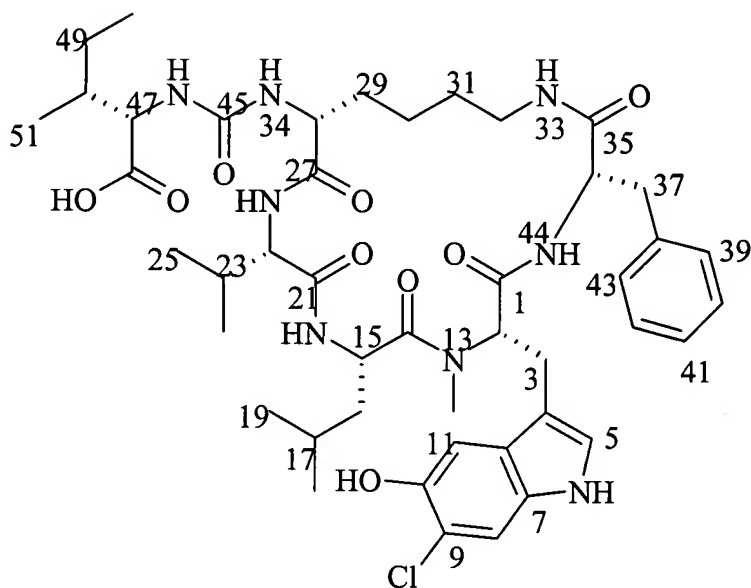
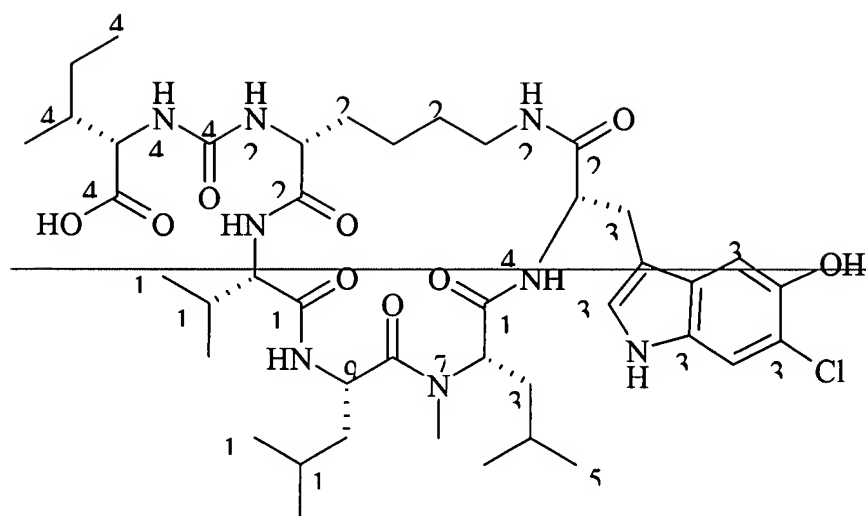
$R^{3a}$  is OH,  $R^{3b}$  is Cl and  $R^{15}$  is H;

$R^{3a}$  is OH,  $R^{3b}$  is Cl and  $R^{15}$  is CH<sub>3</sub>;

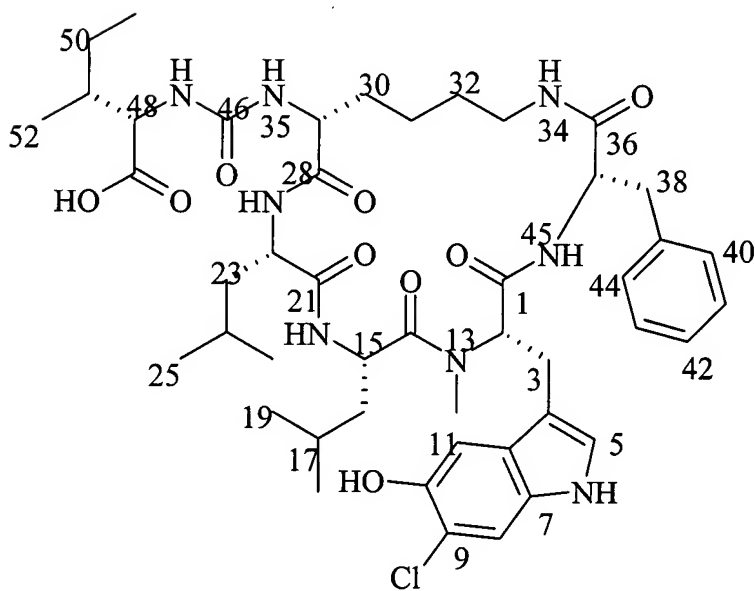
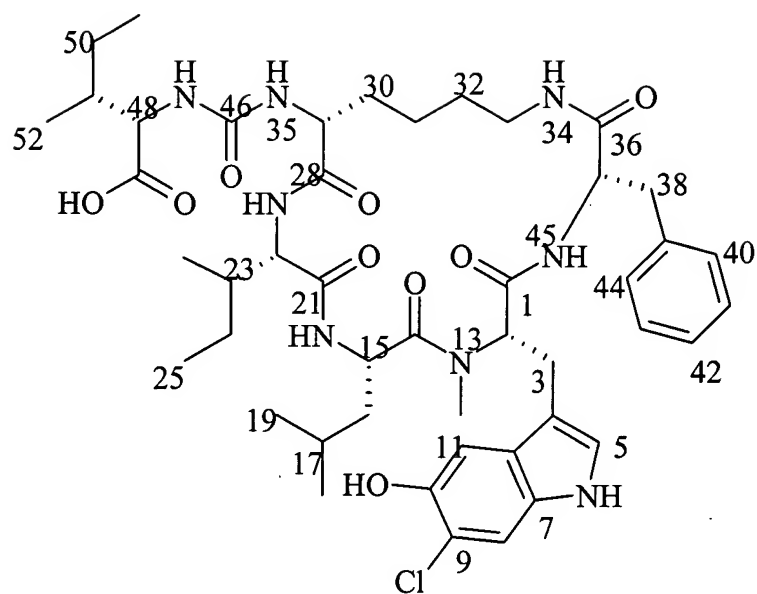
$R^{3a}$  is H,  $R^{3b}$  is H and  $R^{15}$  is CH<sub>3</sub>;

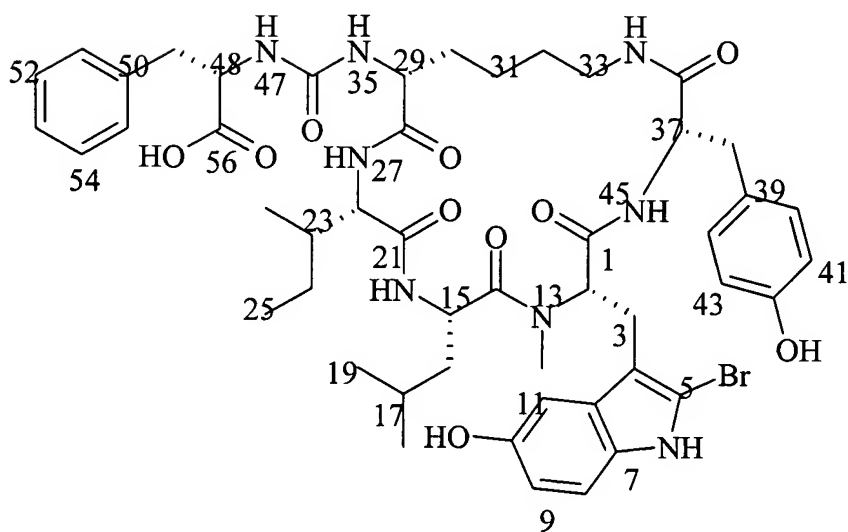
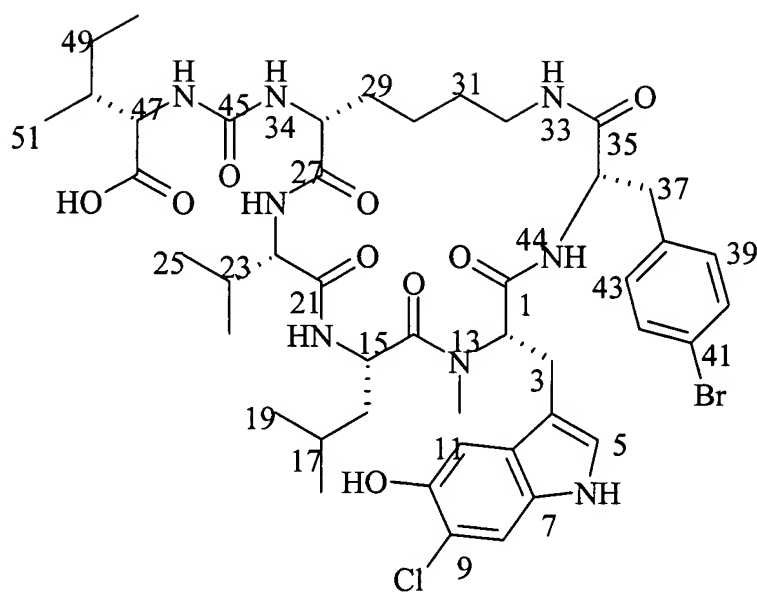
$R^{3a}$  is H,  $R^{3b}$  is Cl and  $R^{15}$  is H;

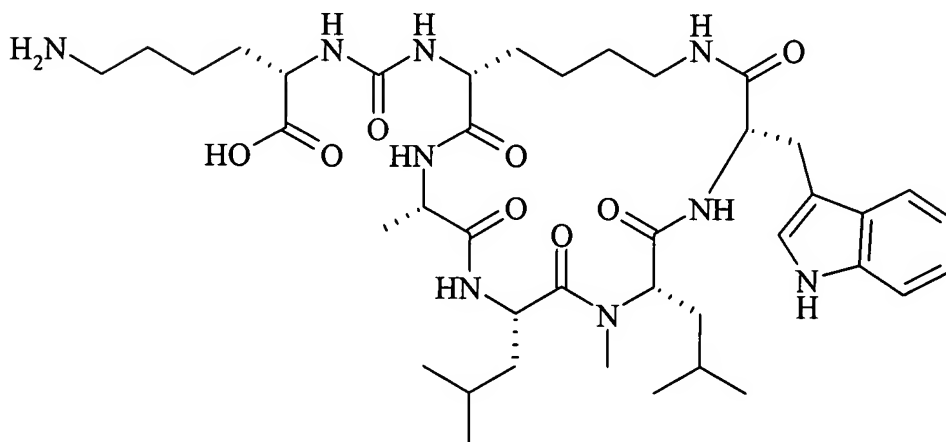
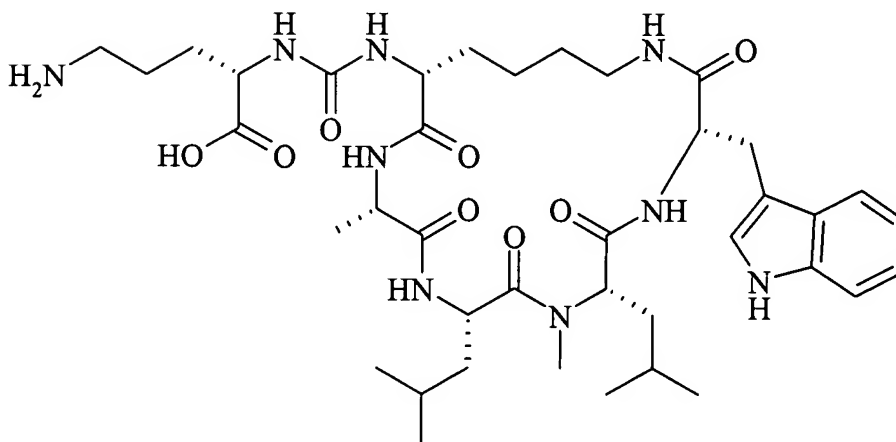
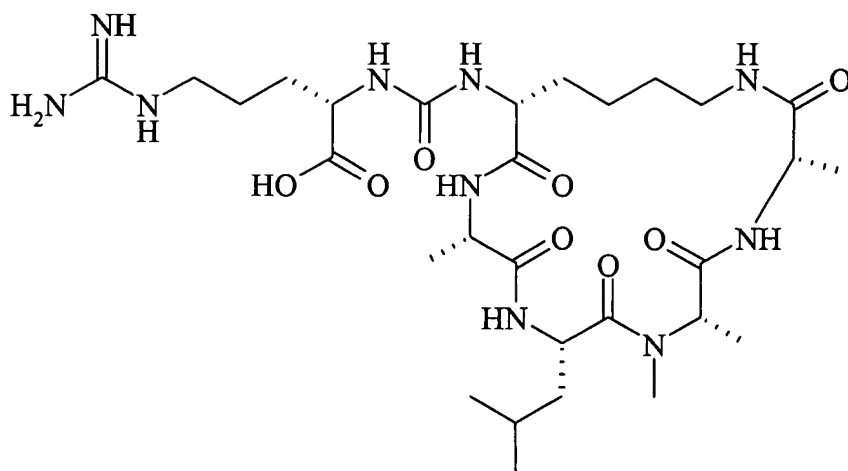


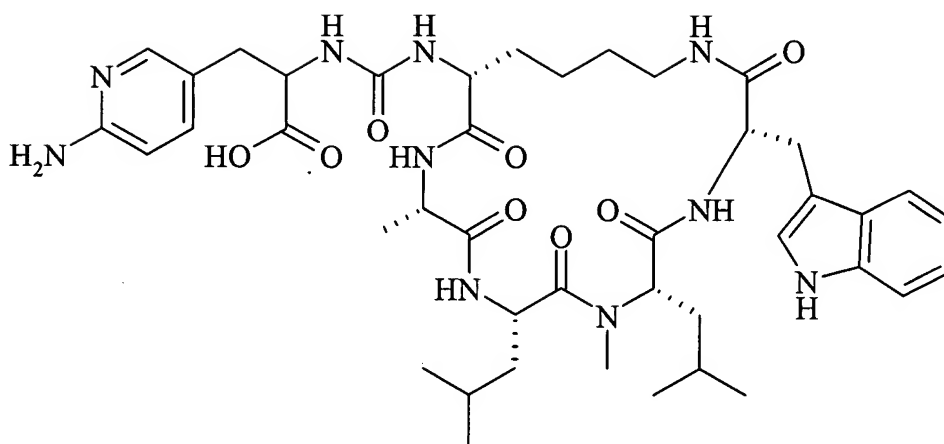




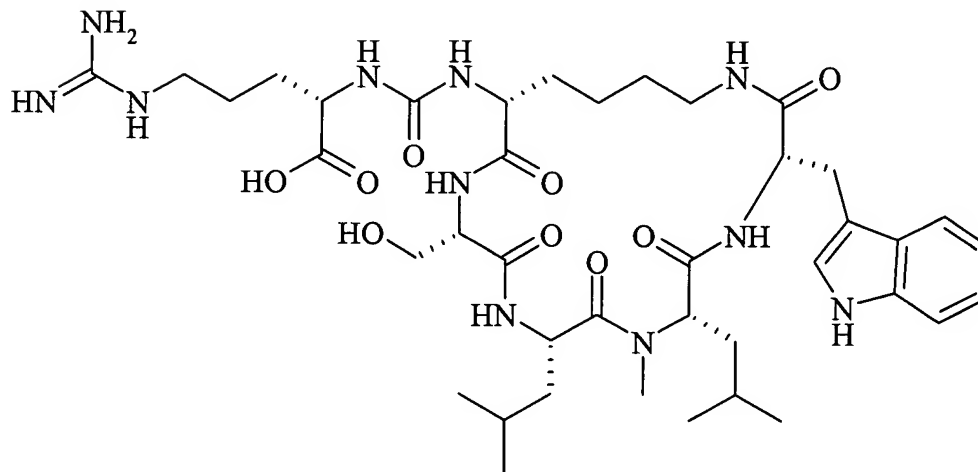








or



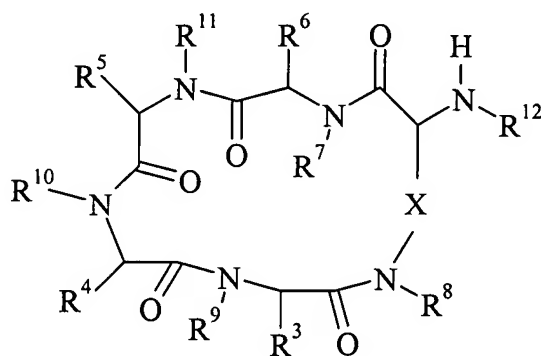
or a pharmaceutically acceptable salt thereof or solvate thereof, or a solvate of a pharmaceutically acceptable salt thereof.

Claim 16 (**currently amended**): A method for the treatment or prophylaxis of a disease or medical condition wherein inhibition of carboxypepsidase U is beneficial, said method comprising administering to a warm-blooded animal in need thereof an effective amount~~The use of a compound of formula (I) or a pharmaceutically acceptable salt thereof or solvate thereof, or a solvate of such a salt; as claimed in claim 2 any one of claims 2 to 15 in a method of manufacturing a medicament for the treatment or prophylaxis of a condition wherein inhibition of carboxypeptidase U is beneficial.~~

Claim 17 (**currently amended**): The method-use as claimed in claim 16 wherein said disease or medical condition is selected from ~~for the manufacture of a medicament for the treatment or prophylaxis of~~ thrombosis and/or hypercoagulability in blood and/or tissues; atherosclerosis; fibrotic conditions; inflammatory diseases; or a condition which benefits from maintaining or enhancing bradykinin levels in the body of a mammal ~~(such as man)~~.

Claim 18 (**currently amended**): A pharmaceutical formulation comprising ~~containing~~ a compound of formula (I) or a pharmaceutically acceptable salt thereof ~~or solvate thereof, or a solvate of such a salt~~; as claimed in claim 2 ~~any one of claims 2 to 15~~ as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent or carrier.

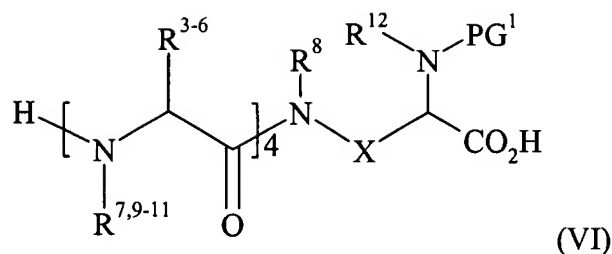
Claim 19 (**currently amended**): A compound of formula



(VII)

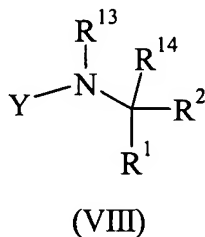
wherein R<sup>3</sup> to R<sup>12</sup> and X are as defined in claim 2 ~~any one of claims 1 to 14~~.

Claim 20 (**currently amended**): A process for preparing a compound as claimed in claim 19 which comprises treating a compound of formula VI ~~in which PG1 is a suitable protecting group with a peptide coupling agent in the presence of a non-nucleophilic base in a polar aprotic solvent and then removing the protecting group.~~



in which PG<sup>1</sup> is a suitable protecting group with a peptide coupling agent in the presence of a non-nucleophilic base in a polar aprotic solvent and then removing the protecting group.

Claim 21 (**currently amended**): A process for preparing a compound of formula I as claimed in claim 2 ~~any one of claims 2 to 17~~ which comprises reacting a compound of formula VII as defined in claim 19 with a compound of formula VIII



in which Y is an activated ester or NY is an isocyanate group.

Claim 22 (**new**): The method as claimed in claim 1 wherein said disease or medical condition is selected from thrombosis and/or hypercoagulability in blood and/or tissues; atherosclerosis; fibrotic conditions; inflammatory diseases; or a condition which benefits from maintaining or enhancing bradykinin levels in the body of a mammal.